```
=> d his

     (FILE 'HOME' ENTERED AT 14:59:11 ON 22 AUG 2006)

     FILE 'REGISTRY' ENTERED AT 14:59:37 ON 22 AUG 2006
                  EXP TIOTROPIUM/CN
L1             10 S E3-E12
                  EXP OXATROPIUM/CN
                  EXP OXITROPIUM/CN
L2              2 S E3-E4
                  EXP IPRATROPIUM/CN
L3              2 S E3-E4
L4              0 S CLIOMILAST/CN
                  EXP ARIFLO/CN
L5              1 S ARIFLO/CN
L6              1 S ENPROFYLLINE/CN
L7              1 S ROFLUMILAST/CN
L8                STRUCTURE UPLOADED
L9              0 S L8
L10            23 S L8 SSS FULL

     FILE 'CAPLUS' ENTERED AT 15:04:11 ON 22 AUG 2006
L11           881 S L1 OR L2 OR L3
L12           556 S L5 OR L6 OR L7 OR L10
L13            26 S L11 AND L12
L14            10 S L13 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONAR
L15             0 S L14 NOT PY>2001
L16             0 S L14 NOT PY>2002
L17           237 S L11 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONAR
L18            51 S L17 NOT PY>2001
L19            11 S L18 AND TIOTROPIUM
L20             0 S L19 AND ASTHSMA
L21             3 S L19 AND ASTHMA
L22             0 S L12 AND ASTHSMA AND (COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONA
L23            85 S L12 AND (COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE
L24            14 S L23 NOT PY>2001

=>
```

```
=> d his

     (FILE 'HOME' ENTERED AT 16:24:23 ON 22 AUG 2006)

     INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
     AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
     CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
     DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 16:24:33 ON 22 AUG 2006
               SEA (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)
               ---------
                1   FILE BIOSIS
                6   FILE CAPLUS
                1   FILE DRUGU
               52   FILE IFIPAT
                2   FILE PHIN
                2   FILE PROMT
                6   FILE PROUSDDR
                1   FILE RDISCLOSURE
                1   FILE SCISEARCH
                1   FILE TOXCENTER
              201   FILE USPATFULL
               27   FILE USPAT2
               32   FILE WPIDS
                6   FILE WPIFV
               32   FILE WPINDEX
                1   FILE DPCI
               36   FILE EPFULL
               16   FILE INPADOC
              305   FILE PCTFULL
L1             QUE (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)
               ---------

     FILE 'USPATFULL, EPFULL, PCTFULL' ENTERED AT 16:26:03 ON 22 AUG 2006
L2          542 S (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)
L3          514 S (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4(W)INHIBIT?)
L4            6 S L3 NOT PY>2001

=>
```

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 21 AUG 2006 HIGHEST RN 903048-34-0
DICTIONARY FILE UPDATES: 21 AUG 2006 HIGHEST RN 903048-34-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

```
=> exp tiotropium/cn
E1            1     TIOTRIAZAZIN/CN
E2            1     TIOTRIFAR/CN
E3            1 --> TIOTROPIUM/CN
E4            1     TIOTROPIUM BROMIDE/CN
E5            1     TIOTROPIUM BROMIDE MONOHYDRATE/CN
E6            1     TIOTROPIUM CHLORIDE/CN
E7            1     TIOTROPIUM HYDROGEN PHOSPHATE/CN
E8            1     TIOTROPIUM IODIDE/CN
E9            1     TIOTROPIUM METHANESULFONATE/CN
E10           1     TIOTROPIUM METHYLSULFATE/CN
E11           1     TIOTROPIUM P-TOLUENESULFONATE/CN
E12           1     TIOTROPIUM PHOSPHATE/CN

=> s E3-E12
              1 TIOTROPIUM/CN
              1 "TIOTROPIUM BROMIDE"/CN
              1 "TIOTROPIUM BROMIDE MONOHYDRATE"/CN
              1 "TIOTROPIUM CHLORIDE"/CN
              1 "TIOTROPIUM HYDROGEN PHOSPHATE"/CN
              1 "TIOTROPIUM IODIDE"/CN
              1 "TIOTROPIUM METHANESULFONATE"/CN
              1 "TIOTROPIUM METHYLSULFATE"/CN
              1 "TIOTROPIUM P-TOLUENESULFONATE"/CN
              1 "TIOTROPIUM PHOSPHATE"/CN
L1           10 (TIOTROPIUM/CN OR "TIOTROPIUM BROMIDE"/CN OR "TIOTROPIUM BROMIDE
                 MONOHYDRATE"/CN OR "TIOTROPIUM CHLORIDE"/CN OR "TIOTROPIUM
                HYDROGEN PHOSPHATE"/CN OR "TIOTROPIUM IODIDE"/CN OR "TIOTROPIUM
                METHANESULFONATE"/CN OR "TIOTROPIUM METHYLSULFATE"/CN OR "TIOTROP
                IUM P-TOLUENESULFONATE"/CN OR "TIOTROPIUM PHOSPHATE"/CN)

=> d l1

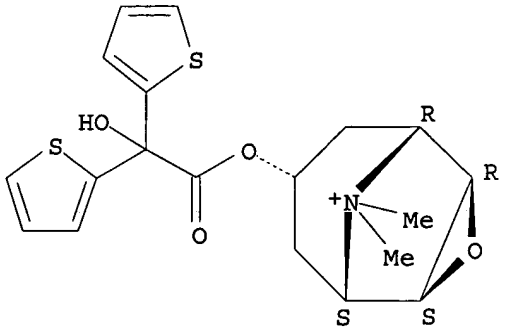
L1   ANSWER 1 OF 10  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   851029-97-5  REGISTRY
ED   Entered STN:  24 May 2005
CN   3-Oxa-9-azoniatricyclo[3.3.1.02,4]nonane, 7-[(hydroxydi-2-
     thienylacetyl)oxy]-9,9-dimethyl-, (1α,2β,4β,5α,7.bet
     a.)-, phosphate (2:1) (salt) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Tiotropium hydrogen phosphate
FS   STEREOSEARCH
```

MF C19 H22 N O4 S2 . 1/2 H O4 P
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

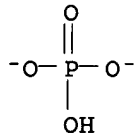
CRN 186691-13-4
CMF C19 H22 N O4 S2

Relative stereochemistry.



CM 2

CRN 14066-19-4
CMF H O4 P



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> exp oxatropium/cn
E1            1     OXATRISTANNETANE/CN
E2            1     OXATRISTANNETANE, HEXAKIS(2,6-DIETHYLPHENYL)-/CN
E3            0 --> OXATROPIUM/CN
E4            1     OXAUNOMYCIN/CN
E5            1     OXAWAX TS 254A/CN
E6            1     OXAWAX TS 254AA/CN
E7            1     OXAYOHIMBAN/CN
E8            1     OXAYOHIMBAN, B-D-GLUCOPYRANOSIDE DERIV./CN
E9            1     OXAYOHIMBAN, 1-PROPANAMINIUM DERIV./CN
E10           1     OXAYOHIMBAN, 16,17-DIDEHYDRO-19-METHYL-, (19A,20.ALPHA
                    .)-(±)-/CN
E11           1     OXAYOHIMBAN, 16,17-DIDEHYDRO-19-METHYL-, (3B,19B)-
                    (±)-/CN
E12           1     OXAYOHIMBAN, 17-METHOXY-19-METHYL-, (17A,19B)-/CN

=> exp oxitropium/cn
E1            1     OXITRIPTAN/CN
E2            1     OXITRIPTYLINE/CN
E3            1 --> OXITROPIUM/CN
E4            1     OXITROPIUM BROMIDE/CN
E5            1     OXIURAN/CN
```

```
E6            1      OXIVENT/CN
E7            1      OXIVOR/CN
E8            1      OXIYANT/CN
E9            1      OXIZINOVOR/CN
E10           1      OXKI 1/CN
E11           1      OXKI 2/CN
E12           1      OXKIL/CN

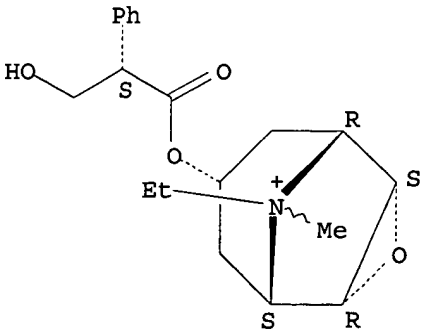
=> s E3=E4
NUMERIC VALUE NOT VALID '"OXITROPIUM BROMIDE"'
Numeric values may contain 1-8 significant figures.  If range notation
is used, both the beginning and the end of the range must be
specified, e.g., '250-300/MW'.  Expressions such as '250-/MW' are not
allowed.  To search for values above or below a given number, use the
>, =>, <, or <= operators, e.g., 'MW => 250'.  Text terms cannot be
used in numeric expressions.  If you specify a unit, it must be
dimensionally correct for that field code.  To see the unit
designations for field codes in the current file, enter "DISPLAY UNIT
ALL" at an arrow prompt (=>).

=> s E3-E4
              1 OXITROPIUM/CN
              1 "OXITROPIUM BROMIDE"/CN
L2            2 (OXITROPIUM/CN OR "OXITROPIUM BROMIDE"/CN)

=> d l2

L2   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   99571-64-9  REGISTRY
ED   Entered STN:  28 Dec 1985
CN   3-Oxa-9-azoniatricyclo[3.3.1.02,4]nonane, 9-ethyl-7-[(2S)-3-hydroxy-1-oxo-
     2-phenylpropoxy]-9-methyl-, (1α,2β,4β,5α,7β)-
     (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   3-Oxa-9-azatricyclo[3.3.1.02,4]nonane, 3-oxa-9-
     azoniatricyclo[3.3.1.02,4]nonane deriv.
CN   3-Oxa-9-azoniatricyclo[3.3.1.02,4]nonane, 9-ethyl-7-(3-hydroxy-1-oxo-2-
     phenylpropoxy)-9-methyl-, [7(S)-(1α,2β,4β,5α,7β
     )]-
OTHER NAMES:
CN   Oxitropium
FS   STEREOSEARCH
MF   C19 H26 N O4
CI   COM
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
```

Absolute stereochemistry.



```
              47 REFERENCES IN FILE CA (1907 TO DATE)
              15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
              48 REFERENCES IN FILE CAPLUS (1907 TO DATE)

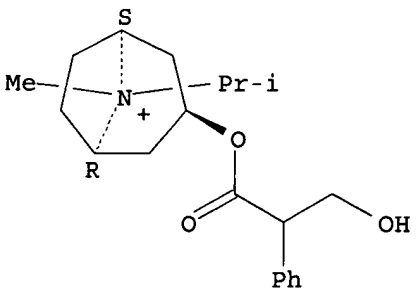

=> exp ipratropium/cn
E1            1     IPRAL SODIUM/CN
E2            1     IPRAMIDIL/CN
E3            1 --> IPRATROPIUM/CN
E4            1     IPRATROPIUM BROMIDE/CN
E5            1     IPRAVACAINE/CN
E6            1     IPRAZID/CN
E7            1     IPRAZIDE/CN
E8            1     IPRAZOCHROME/CN
E9            1     IPRECYNIUM 22/CN
E10           1     IPREN/CN
E11           1     IPRIFLAVONE/CN
E12           1     IPRIFLAVONE-A-CYCLODEXTRIN COMPLEX (1:2)/CN

=> s E3-E4
              1 IPRATROPIUM/CN
              1 "IPRATROPIUM BROMIDE"/CN
L3            2 (IPRATROPIUM/CN OR "IPRATROPIUM BROMIDE"/CN)

=> d l3

L3   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   60205-81-4  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   8-Azoniabicyclo[3.2.1]octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-
     8-(1-methylethyl)-, (3-endo,8-syn)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   8-Azoniabicyclo[3.2.1]octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-
     8-(1-methylethyl)-, (endo,syn)-(±)-
OTHER NAMES:
CN   (±)-Ipratropine
CN   8-Azoniabicyclo[3.2.1]octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-
     8-(1-methylethyl)-, (endo,syn)-
CN   Ipratropium
FS   STEREOSEARCH
DR   197647-02-2
MF   C20 H30 N O3
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS,
       CBNB, CIN, IMSPATENTS, IPA, MEDLINE, PROMT, RTECS*, TOXCENTER, USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)

Relative stereochemistry.
```



```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             196 REFERENCES IN FILE CA (1907 TO DATE)
              20 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             198 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> s cliomilast/cn
L4            0 CLIOMILAST/CN

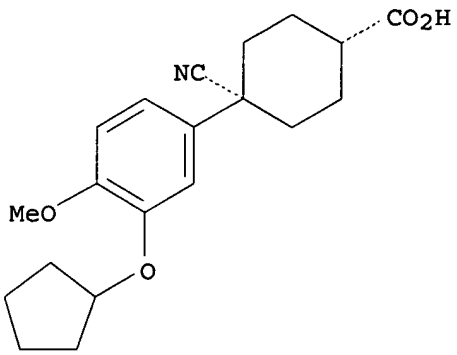
=> exp ariflo/cn
E1            1     ARIETIN (DISINTEGRIN)/CN
E2            1     ARIFEN/CN
E3            1 --> ARIFLO/CN
E4            1     ARIGAL C/CN
E5            1     ARIH1 PROTEIN (MOUSE STRAIN FVB/N CLONE MGC:68355 IMAGE:3498
                    094)/CN
E6            1     ARILAT/CN
E7            1     ARILATE/CN
E8            1     ARILDONE/CN
E9            1     ARILID/CN
E10           1     ARILIN/CN
E11           1     ARILLANIN A/CN
E12           1     ARILLANIN B/CN

=> s ariflo/cn
L5            1 ARIFLO/CN

=> d l5

L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   153259-65-5  REGISTRY
ED   Entered STN:  24 Feb 1994
CN   Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-
     , cis- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Ariflo
CN   Cilomilast
CN   cis-4-Cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexanecarboxylic acid
CN   cis-4-[3-(Cyclopentyloxy)-4-methoxyphenyl]-4-cyanocyclohexane-1-carboxylic
     acid
CN   SB 207499
FS   STEREOSEARCH
MF   C20 H25 N O4
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS,
       CASREACT, CIN, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*,
       PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)

Relative stereochemistry.
```



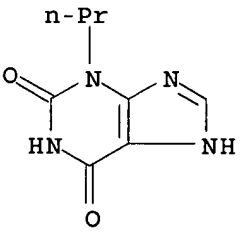
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

200 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
201 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s enprofylline/cn
L6 1 ENPROFYLLINE/CN

=> d l6

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 41078-02-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN 1H-Purine-2,6-dione, 3,7-dihydro-3-propyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3-Propylxanthine
CN D 4028
CN Enprofylline
FS 3D CONCORD
MF C8 H10 N4 O2
LC STN Files: ADISINSIGHT, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



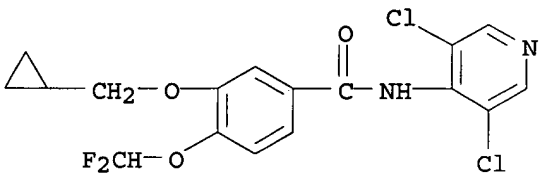
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

304 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
304 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> s roflumilast/cn
L7            1 ROFLUMILAST/CN

=> d l7

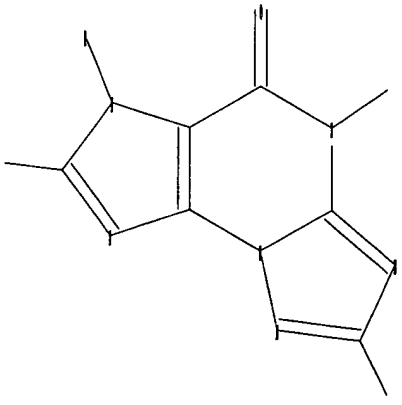
L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   162401-32-3  REGISTRY
ED   Entered STN:  21 Apr 1995
CN   Benzamide, 3-(cyclopropylmethoxy)-N-(3,5-dichloro-4-pyridinyl)-4-
     (difluoromethoxy)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   B 9302-107
CN   BY 217
CN   BYK 20869
CN   Roflumilast
FS   3D CONCORD
MF   C17 H14 Cl2 F2 N2 O3
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS,
       CASREACT, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS,
       IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT, PROUSDDR, RTECS*,
       SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
```

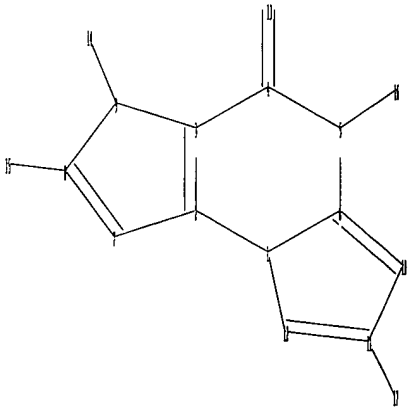



```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             138 REFERENCES IN FILE CA (1907 TO DATE)
              11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             139 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=>
Uploading C:\Program Files\Stnexp\Queries\10613783pde4.str
```





```
chain nodes :
13  14  15  16  17
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12
```

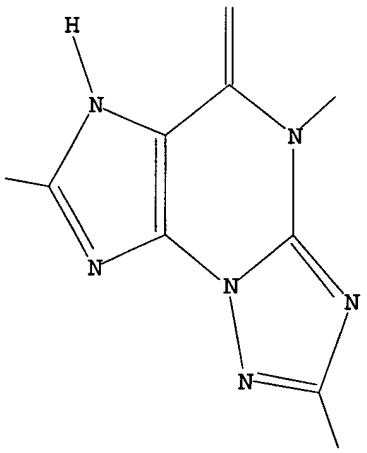
```
chain bonds :
4-13  5-16  8-15  9-14  11-17
ring bonds :
1-2  1-6  1-12  2-3  2-7  3-4  3-9  4-5  5-6  6-10  7-8  8-9  10-11  11-12
exact/norm bonds :
1-2  1-6  1-12  2-3  2-7  3-4  3-9  4-5  4-13  5-6  5-16  6-10  7-8  8-9  10-11
11-12
exact bonds :
8-15  9-14  11-17


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS



L8      STRUCTURE UPLOADED

=> d l8
L8 HAS NO ANSWERS
L8                STR
```




```
Structure attributes must be viewed using STN Express query preparation.


=> s l8
SAMPLE SEARCH INITIATED 15:03:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        6 TO ITERATE

100.0% PROCESSED         6 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            6 TO      266
PROJECTED ANSWERS:               0 TO        0

L9             0 SEA SSS SAM L8

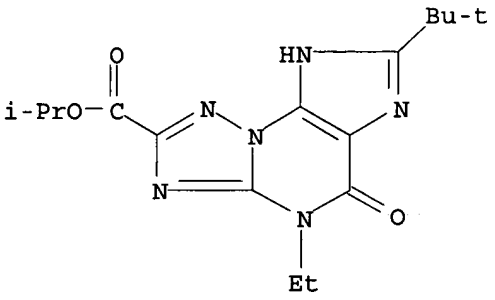
=> s l8 sss full
FULL SEARCH INITIATED 15:03:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      174 TO ITERATE

100.0% PROCESSED       174 ITERATIONS                           23 ANSWERS
SEARCH TIME: 00.00.01
```

L10 23 SEA SSS FUL L8

=> d l10 scan

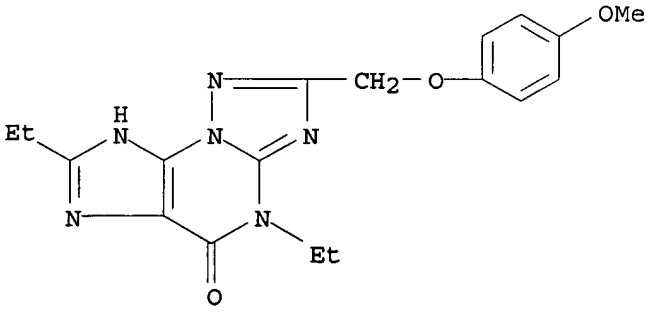
L10 23 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 4H-[1,2,4]Triazolo[5,1-b]purine-2-carboxylic acid, 7-(1,1-dimethylethyl)-4-ethyl-5,6-dihydro-5-oxo-, 1-methylethyl ester (9CI)
MF C16 H22 N6 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

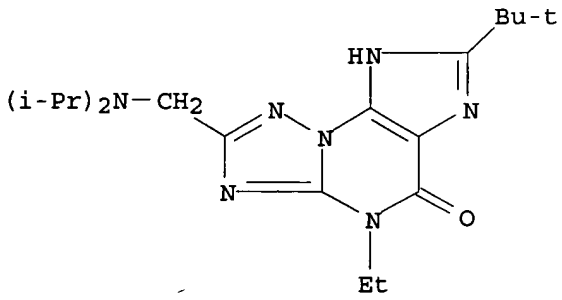
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L10 23 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 4H-[1,2,4]Triazolo[5,1-b]purin-5(6H)-one, 4,7-diethyl-2-[(4-methoxyphenoxy)methyl]- (9CI)
MF C18 H20 N6 O3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L10 23 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 4H-[1,2,4]Triazolo[5,1-b]purin-5(6H)-one, 2-[[bis(1-methylethyl)amino]methyl]-7-(1,1-dimethylethyl)-4-ethyl- (9CI)
MF C19 H31 N7 O



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	267.10	267.31

FILE 'CAPLUS' ENTERED AT 15:04:11 ON 22 AUG 2006
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FILE 'REGISTRY' ENTERED AT 14:59:37 ON 22 AUG 2006
EXP TIOTROPIUM/CN
L1 10 S E3-E12
EXP OXATROPIUM/CN
EXP OXITROPIUM/CN
L2 2 S E3-E4
EXP IPRATROPIUM/CN
L3 2 S E3-E4
L4 0 S CLIOMILAST/CN
EXP ARIFLO/CN
L5 1 S ARIFLO/CN
L6 1 S ENPROFYLLINE/CN

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L7             1 S ROFLUMILAST/CN
L8               STRUCTURE UPLOADED
L9             0 S L8
L10           23 S L8 SSS FULL

     FILE 'CAPLUS' ENTERED AT 15:04:11 ON 22 AUG 2006

=> s L1 or L2 or L3
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            167 L2
            705 L3
L11         881 L1 OR L2 OR L3

=> s L5 or L6 or L7 or L10
            201 L5
            304 L6
            139 L7
              5 L10
L12         556 L5 OR L6 OR L7 OR L10

=> s L11 and L12
L13          26 L11 AND L12

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              0 ASTHSMA
           2718 COPD
         201254 CHRONIC
          11037 OBSTRUCTIVE
          83467 PULMONARY
         880139 DISEASE
           5289 CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE
L14          10 L13 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W
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L16           0 L14 NOT PY>2002

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              0 ASTHSMA
           2718 COPD
         201254 CHRONIC
          11037 OBSTRUCTIVE
          83467 PULMONARY
         880139 DISEASE
           5289 CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE
L17         237 L11 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W
                )DISEASE))

=> s l17 not py>2001
        5196001 PY>2001
L18          51 L17 NOT PY>2001

=> d l18 1-18 ti

L18  ANSWER 1 OF 51  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Asthma medications and their potential adverse effects in the elderly:
     Recommendations for prescribing

L18  ANSWER 2 OF 51  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Pharmacokinetics and tissue distribution of the anticholinergics
```

tiotropium and ipratropium in the rat and dog

L18 ANSWER 3 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Ipratropium bromide hydrofluoroalkane inhalation aerosol is safe and effective in patients with COPD

L18 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Effective delivery of particles with the HandiHaler dry powder inhalation system over a range of chronic obstructive pulmonary disease severity

L18 ANSWER 5 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Management of acute exacerbations of chronic obstructive pulmonary disease

L18 ANSWER 6 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Effectiveness of salmeterol versus ipratropium bromide on exertional dyspnea in COPD

L18 ANSWER 7 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Inhaled salmeterol: A review of its efficacy in chronic obstructive pulmonary disease

L18 ANSWER 8 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI In patients with COPD, treatment with a combination of formoterol and ipratropium is more effective than a combination of salbutamol and ipratropium: A 3-week, randomized, double-blind, within-patient, multicenter study

L18 ANSWER 9 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Antimuscarinic treatment for lung diseases. From research to clinical practice

L18 ANSWER 10 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Anticholinergics: Tiotropium

L18 ANSWER 11 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tiotropium bromide

L18 ANSWER 12 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Systemic glucocorticoids in severe exacerbations of COPD

L18 ANSWER 13 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Effect of ipratropium bromide on airway and pulmonary muscarinic receptors in a rat model of chronic obstructive pulmonary disease

L18 ANSWER 14 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI The impact of combined inhaled bronchodilator therapy in the treatment of COPD

L18 ANSWER 15 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Inhaled anticholinergic therapy: applied pharmacology and interesting developments

L18 ANSWER 16 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Anticholinergic bronchodilators in combination

L18 ANSWER 17 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tiotropium bromide: treatment of COPD, bronchodilator, muscarinic antagonist

L18 ANSWER 18 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN
TI Long-term treatment of chronic obstructive pulmonary disease with salmeterol and the additive

effect of ipratropium

=> s l18 and tiotropium
289 TIOTROPIUM
L19 11 L18 AND TIOTROPIUM

=> d l19 1-11 ti

L19 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Pharmacokinetics and tissue distribution of the anticholinergics tiotropium and ipratropium in the rat and dog

L19 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Effective delivery of particles with the HandiHaler dry powder inhalation system over a range of chronic obstructive pulmonary disease severity

L19 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Antimuscarinic treatment for lung diseases. From research to clinical practice

L19 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Anticholinergics: Tiotropium

L19 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tiotropium bromide

L19 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Inhaled anticholinergic therapy: applied pharmacology and interesting developments

L19 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tiotropium bromide: treatment of COPD, bronchodilator, muscarinic antagonist

L19 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tiotropium (Ba 679): Pharmacology and early clinical observations

L19 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tiotropium (Spiriva): mechanistical considerations and clinical profile in obstructive lung disease

L19 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tiotropium bromide, a new long-acting antimuscarinic bronchodilator: a pharmacodynamic study in patients with chronic obstructive pulmonary disease (COPD)

L19 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
TI Tiotropium bromide (Ba 679 BR), a novel long-acting muscarinic antagonist for the treatment of obstructive airways disease

=> d l19 1 2 4 5 6 7 8 9 10 11

L19 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:936981 CAPLUS
DN 136:210019
TI Pharmacokinetics and tissue distribution of the anticholinergics tiotropium and ipratropium in the rat and dog
AU Leusch, A.; Eichhorn, B.; Muller, G.; Rominger, K.-L.
CS Department of Pharmacokinetics and Drug Metabolism, Boehringer Ingelheim Pharma KG, Biberach, 88397, Germany
SO Biopharmaceutics & Drug Disposition (2001), 22(5), 199-212

CODEN: BDDID8; ISSN: 0142-2782
PB John Wiley & Sons Ltd.
DT Journal
LA English
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:689613 CAPLUS
DN 136:390861
TI Effective delivery of particles with the HandiHaler dry powder inhalation system over a range of chronic obstructive pulmonary disease severity
AU Chodosh, Sanford; Flanders, Judith S.; Kesten, Steven; Serby, Charles W.; Hochrainer, Dieter; Witek, Theodore J., Jr.
CS Veterans Administration Outpatient Clinic, Pulmonary Research, Boston, MA, USA
SO Journal of Aerosol Medicine (2001), 14(3), 309-315
CODEN: JAEMEP; ISSN: 0894-2684
PB Mary Ann Liebert, Inc.
DT Journal
LA English
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:360977 CAPLUS
DN 135:235691
TI Anticholinergics: Tiotropium
AU Disse, Bernd; Witek, Theodore J., Jr.
CS Clinical Research Institute, Boehringer Ingelheim, Ingelheim/Rhein, Germany
SO Progress in Respiratory Research (2001), 31(New Drugs for Asthma, Allergy and COPD), 72-76
CODEN: PRRRAE; ISSN: 1422-2140
PB S. Karger AG
DT Journal; General Review
LA English
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:266014 CAPLUS
DN 135:40286
TI Tiotropium bromide
AU Barnes, Peter J.
CS Department of Thoracic Medicine, National Heart and Lung Institute, Imperial College, London, UK
SO Expert Opinion on Investigational Drugs (2001), 10(4), 733-740
CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:65653 CAPLUS
DN 135:86394
TI Inhaled anticholinergic therapy: applied pharmacology and interesting developments
AU Witek, Theodore J., Jr.; Disse, Bernd
CS Head, Respiratory & Immunology Clinical Research, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877-0363, USA
SO Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(1),

53-58
CODEN: COIDAZ
PB PharmaPress Ltd.
DT Journal; General Review
LA English
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:717146 CAPLUS
DN 134:260728
TI Tiotropium bromide: treatment of COPD, bronchodilator, muscarinic antagonist
AU Norman, P.; Graul, A.; Rabasseda, X.; Castaner, J.
CS Bucks, SL1 8JW, UK
SO Drugs of the Future (2000), 25(7), 693-699
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:53706 CAPLUS
DN 132:73121
TI Tiotropium (Ba 679): Pharmacology and early clinical observations
AU Witek, Theodore J., Jr.; Souhrada, Joseph F.; Serby, Charles W.; Disse, Bernd
CS Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA
SO Lung Biology in Health and Disease (1999), 134(Anticholinergic Agents in the Upper and Lower Airways), 137-152
CODEN: LBHDD7; ISSN: 0362-3181
PB Marcel Dekker, Inc.
DT Journal; General Review
LA English
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:87226 CAPLUS
DN 130:261837
TI Tiotropium (Spiriva): mechanistical considerations and clinical profile in obstructive lung disease
AU Disse, Bernd; Speck, Georg A.; Rominger, Karl Ludwig; Witek, Theodore J., Jr.; Hammer, Rudolf
CS Corporate Medical Division and R&D Division, Boehringer Ingelheim, Ingelheim, 55216, Germany
SO Life Sciences (1999), 64(6/7), 457-464
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:971815 CAPLUS
DN 124:76095
TI Tiotropium bromide, a new long-acting antimuscarinic bronchodilator: a pharmacodynamic study in patients with chronic obstructive pulmonary disease (COPD)
AU Maesen, F. P. V.; Smeets, J. J.; Sledsens, T. J. H.; Wald, F. D. M.; Cornelissen, P. J. G.

CS Dept. Respiratory Diseases, De Wever Hospital, Heerlen, Neth.
SO European Respiratory Journal (1995), 8(9), 1506-13
CODEN: ERJOEI; ISSN: 0903-1936
PB Munksgaard
DT Journal
LA English

L19 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:381396 CAPLUS
DN 122:151131
TI Tiotropium bromide (Ba 679 BR), a novel long-acting muscarinic antagonist for the treatment of obstructive airways disease
AU Barnes, Peter J.; Belvisi, Maria G.; Mak, Judith CW; Haddad, El-Bdaoui; O'Connor, Brian
CS Dep. Thoracic Med., Natl. Heart Lung Inst., London, SW3 6LY, UK
SO Life Sciences (1995), 56(11/12), 853-60
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier
DT Journal
LA English

=> s l19 and asthsma
0 ASTHSMA
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=> s l19 and asthma
31962 ASTHMA
L21 3 L19 AND ASTHMA

=> d l21 1-3

L21 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:65653 CAPLUS
DN 135:86394
TI Inhaled anticholinergic therapy: applied pharmacology and interesting developments
AU Witek, Theodore J., Jr.; Disse, Bernd
CS Head, Respiratory & Immunology Clinical Research, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877-0363, USA
SO Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(1), 53-58
CODEN: COIDAZ
PB PharmaPress Ltd.
DT Journal; General Review
LA English
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:87226 CAPLUS
DN 130:261837
TI Tiotropium (Spiriva): mechanistical considerations and clinical profile in obstructive lung disease
AU Disse, Bernd; Speck, Georg A.; Rominger, Karl Ludwig; Witek, Theodore J., Jr.; Hammer, Rudolf
CS Corporate Medical Division and R&D Division, Boehringer Ingelheim, Ingelheim, 55216, Germany
SO Life Sciences (1999), 64(6/7), 457-464
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L21  ANSWER 3 OF 3  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   1995:381396  CAPLUS
DN   122:151131
TI   Tiotropium bromide (Ba 679 BR), a novel long-acting muscarinic
     antagonist for the treatment of obstructive airways disease
AU   Barnes, Peter J.; Belvisi, Maria G.; Mak, Judith CW; Haddad, El-Bdaoui;
     O'Connor, Brian
CS   Dep. Thoracic Med., Natl. Heart Lung Inst., London, SW3 6LY, UK
SO   Life Sciences (1995), 56(11/12), 853-60
     CODEN: LIFSAK; ISSN: 0024-3205
PB   Elsevier
DT   Journal
LA   English


=> s L11 and asthsma and COPD or (chronic(w)obstructive(w)pulmonary(w)disease))
UNMATCHED RIGHT PARENTHESIS 'DISEASE))'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s L12 and asthsma and (COPD or (chronic(w)obstructive(w)pulmonary(w)disease))
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         83467 PULMONARY
        880139 DISEASE
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L24         14 L23 NOT PY>2001

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L24  ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Warfarin pharmacodynamics unaffected by cilomilast

L24  ANSWER 2 OF 14  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Cilomilast, a selective phosphodiesterase-4 inhibitor for treatment of
     patients with chronic obstructive pulmonary
     disease: a randomised, dose-ranging study

L24  ANSWER 3 OF 14  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   The next generation of PDE4 inhibitors

L24  ANSWER 4 OF 14  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Cilomilast: a second generation phosphodiesterase 4 inhibitor for asthma
     and chronic obstructive pulmonary
     disease

L24  ANSWER 5 OF 14  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   In vivo efficacy in airway disease models of roflumilast, a novel orally
```

active PDE4 inhibitor

L24 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro

L24 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Roflumilast: antiallergy/antiasthmatic, treatment of COPD, phosphodiesterase 4 inhibitor

L24 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Chronic obstructive pulmonary disease: emerging therapies

L24 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Low-adenosine antisense oligonucleotide agents, compositions, kits and treatments for respiratory disorders

L24 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Ariflo SmithKline Beecham

L24 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Ariflo SmithKline Beecham plc

L24 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI AriflоTM(SB 207499), a second generation phosphodiesterase 4 inhibitor for the treatment of asthma and COPD: from concept to clinic

L24 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI SB-207499 SmithKline Beecham plc

L24 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI SB-207499. antiasthmatic/antiinflammatory, phosphodiesterase IV inhibitor

=> d l24 2 4 5 6 7 8 10 11 12 13 14 ti abs bib

L24 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Cilomilast, a selective phosphodiesterase-4 inhibitor for treatment of patients with chronic obstructive pulmonary disease: a randomised, dose-ranging study
AB Background Chronic obstructive pulmonary disease (COPD) is a common, progressive respiratory disease that causes great morbidity and mortality despite treatment. There is evidence for airway inflammation in COPD. Cilomilast is an orally active, potent, selective phosphodiesterase type 4 inhibitor, which in vitro can affect cells thought to be of clin. importance in COPD. The authors' aim was to assess the safety, efficacy, and dose response of cilomilast in the treatment of patients with this disease. Methods The authors did a 6-wk, randomized, dose-ranging study in 424 patients with COPD (forced expiratory volume in 1 s [FEV1] 46·8% of predicted, FEV1/forced vital capacity [FVC] 54·6%, and postsalbutamol reversibility 5·4%). The authors randomly assigned individuals at 60 European centers to receive cilomilast 5 (n=109), 10 (n=102), or 15 (n=107) mg twice daily, or placebo (n=106). The main outcome measure was trough FEV1 before and after use of a bronchodilator. Analyses were by intention to treat. Findings Cilomilast 15 mg twice daily significantly improved FEV1 compared with placebo (mean 130 mL vs -30 mL [95% CI 90-240] at week 6). FVC and peak expiratory flow were also improved. Quality of life measures did not differ significantly between the groups. There were no significant differences in serious adverse events between the groups. Interpretation Cilomilast 15 mg twice daily might be an effective maintenance treatment for COPD. Further clin. studies are underway.
AN 2001:574024 CAPLUS

DN 136:319139
TI Cilomilast, a selective phosphodiesterase-4 inhibitor for treatment of patients with chronic obstructive pulmonary disease: a randomised, dose-ranging study
AU Compton, C. H.; Gubb, J.; Nieman, R.; Edelson, J.; Amit, O.; Bakst, A.; Ayres, J. G.; Creemers, J. P. H. M.; Schultze-Werninghaus, G.; Brambilla, C.; Barnes, N. C.
CS International Study Group, Department of SmithKline Beecham Pharmaceuticals, Harlow, UK
SO Lancet (2001), 358(9278), 265-270
CODEN: LANCAO; ISSN: 0140-6736
PB Lancet Ltd.
DT Journal
LA English
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Cilomilast: a second generation phosphodiesterase 4 inhibitor for asthma and chronic obstructive pulmonary disease
AB A review with 126 refs. Cilomilast (Ariflo, SB-207499) is an orally-active, second generation phosphodiesterase (PDE) inhibitor that may be effective in the treatment of asthma and chronic obstructive pulmonary disease (COPD). It has high selectivity for the cAMP-specific, or PDE4, isoenzyme that predominates in pro-inflammatory and immune cells and is ten-fold more selective for PDE4D than for PDE4A, B and C. In vitro, cilomilast suppresses the activity of many pro-inflammatory and immune cells that have been implicated in the pathogenesis of asthma and COPD and is highly active in animal models of these diseases. Cilomilast demonstrates a markedly improved side effect profile over the archetypal PDE4 inhibitor, rolipram, which has been attributed to its inability to discriminate between the high affinity rolipram binding site and the catalytic domain of the enzyme, and the fact that it is neg. charged which at physiol. pH should limit its penetration in to the CNS. In humans cilomilast is rapidly absorbed after oral administration, providing dose-proportional systemic exposure up to 4 mg, completely bioavailable, has a half-life of .apprx. 7 h and is subject to negligible first pass hepatic metabolism Cilomilast is extensively metabolized with decyclopentylation, acyl glucuronidation and 3-hydroxylation of the cyclopentyl ring representing the principal routes. Most of the drug is excreted in the urine (.apprx. 90%) and feces (6 - 7%) with unchanged cilomilast accounting for less than 1% of the administered dose. Cilomilast has been evaluated in Phase I, Phase II and Phase III trials and dose-response expts. have demonstrated a clin. significant increase in lung function and a perceived improvement in quality of life in patients with COPD. Trials of cilomilast in asthma have been less impressive although a trend towards improved lung function has been reported. Cilomilast is safe and well-tolerated at doses up to 15 mg in both short- and long-term dosing trials with a low incidence of adverse effects. No evidence for drug-drug interactions with commonly prescribed medications for COPD and asthma such as digoxin, corticosteroids, salbutamol, theophylline or warfarin has been found. Moreover, the pharmacokinetics of cilomilast are essentially the same in smokers and non-smokers, indicating that no dose adjustments of cilomilast will be required in patients with COPD. Thus, cilomilast displays a promising clin. profile in the treatment of inflammatory airway diseases, in particular COPD and the results of further Phase III trials are awaited with interest.
AN 2001:522203 CAPLUS
DN 135:220550
TI Cilomilast: a second generation phosphodiesterase 4 inhibitor for asthma and chronic obstructive pulmonary disease

AU Giembycz, Mark A.
CS Thoracic Medicine, National Heart & Lung Institute, Imperial College School of Medicine, London, UK
SO Expert Opinion on Investigational Drugs (2001), 10(7), 1361-1379
CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
RE.CNT 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI In vivo efficacy in airway disease models of roflumilast, a novel orally active PDE4 inhibitor
AB We have investigated the bronchodilator and anti-inflammatory properties of roflumilast (3-cyclopropylmethoxy-4-difluoromethoxy-N-[3,5-dichloropyrid-4-yl]-b enzamide), a novel, highly potent, and selective phosphodiesterase 4 (PDE4) inhibitor. Addnl., we compared the effects of roflumilast and its N-oxide, the primary metabolite in vivo, with those of the PDE4 inhibitors piclamilast, rolipram, and cilomilast. Roflumilast inhibited the ovalbumin-evoked contractions of tracheal chains prepared from sensitized guinea pigs (EC50 = 2+10-7 M) but showed no relaxant effect on tissues contracted spontaneously. In spasmogen-challenged rats and guinea pigs, i.v. administered roflumilast displayed bronchodilatory activity (ED50 = 4.4 and 7.1 μmol/kg, resp.). Furthermore, roflumilast dose dependently attenuated allergen-induced bronchoconstriction in guinea pigs (ED50 = 0.1 μmol/kg i.v.). Roflumilast given orally (ED50 = 1.5 μmol/kg) showed equal potency to its N-oxide (ED50 = 1.0 μmol/kg) but was superior to piclamilast (ED50 = 8.3 μmol/kg), rolipram (ED50 = 32.5 μmol/kg), and cilomilast (ED50 = 52.2 μmol/kg) in suppressing allergen-induced early airway reactions. To assess the anti-inflammatory potential of orally administered roflumilast, antigen-induced cell infiltration, total protein, and TNFα concentration in bronchoalveolar lavage fluid of Brown Norway rats were determined Roflumilast and its N-oxide equally inhibited eosinophilia (ED50 = 2.7 and 2.5 μmol/kg, resp.), whereas the reference inhibitors displayed lower potency (ED50 = 17-106 μmol/kg). Besides, orally administered roflumilast abrogated LPS-induced circulating TNFα in the rat (ED50 = 0.3 μmol/kg), an effect shared by its N-oxide, with both mols. exhibiting 8-, 25-, and 310-fold superiority to piclamilast, rolipram, and cilomilast, resp. These results, coupled with the in vitro effects of roflumilast on inflammatory cells, suggest that roflumilast represents a potential new drug for the treatment of asthma and chronic obstructive pulmonary disease.
AN 2001:240840 CAPLUS
DN 135:86928
TI In vivo efficacy in airway disease models of roflumilast, a novel orally active PDE4 inhibitor
AU Bundschuh, Daniela S.; Eltze, Manfrid; Barsig, Johannes; Wollin, Lutz; Hatzelmann, Armin; Beume, Rolf
CS Department of Pharmacology, Byk Gulden, Konstanz, Germany
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(1), 280-290
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro
AB From a series of benzamide derivs., roflumilast (3-cyclopropylmethoxy-4-difluoromethoxy-N-[3,5-di-chloropyrid-4-yl]b enzamide) was identified as a

potent and selective PDE4 inhibitor. It inhibits PDE4 activity from human neutrophils with an IC50 of 0.8 nM without affecting PDE1 (bovine brain), PDE2 (rat heart), and PDE3 and PDE5 (human platelets) even at 10,000-fold higher concns. Roflumilast is almost equipotent to its major metabolite formed in vivo (roflumilast N-oxide) and piclamilast (RP 73401), however, more than 100-fold more potent than rolipram and Ariflo (cilomilast; SB 207499). The anti-inflammatory and immunomodulatory potential of roflumilast and the reference compds. was investigated in various human leukocytes using cell-specific responses: neutrophils [N-formyl-methyl-leucyl-phenylalanine (fMLP)-induced formation of LTB4 and reactive oxygen species (ROS)], eosinophils (fMLP- and C5a-induced ROS formation), monocytes, monocyte-derived macrophages, and dendritic cells (lipopolysaccharide-induced tumor necrosis factor-α synthesis), and CD4+ T cells (anti-CD3/anti-CD28 monoclonal antibody-stimulated proliferation, IL-2, IL-4, IL-5, and interferon-γ release). Independent of the cell type and the response investigated, the corresponding IC values (for half-maximum inhibition) of roflumilast were within a narrow range (2-21 nM), very similar to roflumilast N-oxide (3-40 nM) and piclamilast (2-13 nM). In contrast, cilomilast (40-3000 nM) and rolipram (10-600 nM) showed greater differences with the highest potency for neutrophils. Compared with neutrophils and eosinophils, representing the terminal inflammatory effector cells, the relative potency of roflumilast and its N-oxide for monocytes, CD4+ T cells, and dendritic cells is substantially higher compared with cilomilast and rolipram, probably reflecting an improved immunomodulatory potential. The efficacy or roflumilast in vitro and in vivo (see accompanying article in this issue) suggests that roflumilast will be useful in the treatment of chronic inflammatory disorders such as asthma and chronic obstructive pulmonary disease.

AN 2001:240839 CAPLUS
DN 135:28819
TI Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro
AU Hatzelmann, Armin; Schudt, Christian
CS Department of Biochemistry, Byk Gulden, Konstanz, Germany
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(1), 267-279
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Roflumilast: antiallergy/antiasthmatic, treatment of COPD, phosphodiesterase 4 inhibitor
AB A review with 16 refs. regarding the drug roflumilast which is used to treat chronic obstructive pulmonary disease (COPD) and asthma. Topics discussed include its synthesis, description, pharmacol. actions, and clin. studies.
AN 2001:196352 CAPLUS
DN 135:161992
TI Roflumilast: antiallergy/antiasthmatic, treatment of COPD, phosphodiesterase 4 inhibitor
AU Sorbera, L. A.; Leeson, P. A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2000), 25(12), 1261-1264
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Chronic obstructive pulmonary disease: emerging therapies
AB A review with 60 refs. Despite the high prevalence of and mortality from chronic obstructive pulmonary disease, extensive research on the underlying pathophysiol. and specific therapeutics for this disease is, relatively, in its infancy. Several novel mol. targets are being investigated as potential treatments for the disease. The most exciting new class of compds. is the phosphodiesterase 4 inhibitors; Ariflo (SB 207499) - a member of this class, and the most advanced in development (Phase III) - was reported recently to have significant clin. efficacy in patients with chronic obstructive pulmonary disease. Phosphodiesterase 4 inhibitors, such as Ariflo, possibly represent the most important advance in pulmonary medicine in recent years.
AN 2000:584132 CAPLUS
DN 133:246695
TI Chronic obstructive pulmonary disease: emerging therapies
AU Hay, Douglas W. P.
CS Department of Pulmonary Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SO Current Opinion in Chemical Biology (2000), 4(4), 412-419
CODEN: COCBF4; ISSN: 1367-5931
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Ariflo SmithKline Beecham
AB A review with .apprx.120 refs. Ariflo (SB-207499) is a phosphodiesterase (PDE)4 inhibitor under development by SmithKline Beecham and in phase III and II clin. trials as a potential treatment for chronic obstructive pulmonary disease (COPD) and asthma, resp. It has commenced phase II trials as a treatment for bronchial asthma in Japan. In Feb. 1999, Merrill Lynch predicted that Ariflo would be launched by the end of 2000 or early 2001 with first year sales of UK £25 million rising to UK £175 million in 2003. In July 1999, Merrill Lynch forecast filing of Ariflo by the second half of 2000. In Feb. 1999, ABN Amro predicted sales of UK £52 million in 2001, rising to UK £254 million in 2005.
AN 1999:732844 CAPLUS
DN 132:202457
TI Ariflo SmithKline Beecham
AU Brown, William
CS Somerville, NJ, 08876-8139, USA
SO Current Opinion in Cardiovascular, Pulmonary & Renal Investigational Drugs (1999), 1(4), 506-515
CODEN: CCPRFX; ISSN: 1464-8482
PB Current Drugs Ltd.
DT Journal; General Review
LA English
RE.CNT 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI Ariflo SmithKline Beecham plc
AB A review with 136 refs. Ariflo (SB-207499) is a phosphodiesterase (PDE)4 inhibitor under development by SmithKline Beecham and in phase III and II clin. trials as a potential treatment for chronic obstructive pulmonary disease (COPD) and asthma, resp. [284490]. It has commenced phase II trials as a treatment for bronchial asthma in Japan [248285,300145]. In Feb. 1999,

Merrill Lynch predicted that Ariflo would be launched by the end of 2000 or early 2001 with first year sales of UK £25 million rising to UK £175 million in 2003 [300257,314372]. In Feb. 1999 ABN Amro predicted sales of UK £52 million in 2001 rising to UK £254 million in 2005 [317577,328676].

AN 1999:609466 CAPLUS
DN 131:222870
TI Ariflo SmithKline Beecham plc
AU Brown, William
CS Somerville, NJ, 08876-8139, USA
SO IDrugs (1999), 2(9), 915-924
CODEN: IDRUFN; ISSN: 1369-7056
PB Current Drugs Ltd.
DT Journal; General Review
LA English
RE.CNT 135 THERE ARE 135 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI AriflоTM(SB 207499), a second generation phosphodiesterase 4 inhibitor for the treatment of asthma and COPD: from concept to clinic
AB A review with 22 refs. on efficacy and safety of the title PDE4 inhibitor in the treatment of pulmonary diseases. (c) 1999 Academic Press.
AN 1999:387455 CAPLUS
DN 131:222898
TI AriflоTM(SB 207499), a second generation phosphodiesterase 4 inhibitor for the treatment of asthma and COPD: from concept to clinic
AU Torphy, T. J.; Barnette, M. S.; Underwood, D. C.; Griswold, D. E.; Christensen, S. B.; Murdoch, R. D.; Nieman, R. B.; Compton, C. H.
CS Division of Cardiovascular and Pulmonary Research, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SO Pulmonary Pharmacology & Therapeutics (1999), 12(2), 131-135
CODEN: PPTHFJ; ISSN: 1094-5539
PB Academic Press
DT Journal; General Review
LA English
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI SB-207499 SmithKline Beecham plc
AB A review with many refs. SB-207499 (Ariflo) is a phosphodiesterase type 4 (PDE4) inhibitor under development by SmithKline Beecham; the drug is in phase III and II clin. trials as a potential treatment for chronic obstructive pulmonary disease (COPD) and asthma, resp. The company has also begun phase II trials as a treatment for bronchial asthma in Japan. In Feb. 1999 Merrill Lynch predicted that Ariflo would be launched by the end of 2000 or early 2001 with first year sales of STG 25 million rising to STG 175 million in 2003. In Feb. 1999 ABN Amro predicted sales of STG 52 million in 2001 rising to STG 254 million in 2005.
AN 1999:339256 CAPLUS
DN 131:138792
TI SB-207499 SmithKline Beecham plc
AU Brown, William M.
CS Department of Anatomy & Physiology, University of Tasmania, Hobart, Australia
SO Current Opinion in Anti-Inflammatory and Immunomodulatory Investigational Drugs (1999), 1(1), 39-47
CODEN: COAIFF; ISSN: 1464-8474
PB Current Drugs Ltd.
DT Journal; General Review
LA English
RE.CNT 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
TI SB-207499. antiasthmatic/antiinflammatory, phosphodiesterase IV inhibitor
AB A brief review with 49 refs. is given on cis-4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]cyclohexane-1-carboxylic acid, SB-207499, ariflo, selected for treating allergic and inflammatory diseases. The 2nd-generation phosphodiesterase (PDE) 4 inhibitor SB-207499 under development is compared with corresponding drugs like rolipram, atizoram, piclamilast, V-11294A, and T-440. The PDE 4 inhibitory activities, the high-affinity rolipram binding site, the in vitro inhibitory activities on tumor necrosis factor-α production, on bronchoconstriction, and on cloned human PDE 4 subtypes are compared. Pharmacol. actions, pharmacokinetics, pharmacodynamics, and clin. studies are described. SB-207499 is currently in phase II testing in adults and pediatric patients with asthma and in phase III trials in patients with chronic obstructive pulmonary disease.
AN 1998:616407 CAPLUS
DN 130:79
TI SB-207499. antiasthmatic/antiinflammatory, phosphodiesterase IV inhibitor
AU Silvestre, J.; Graul, A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (1998), 23(6), 607-615
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 14:59:11 ON 22 AUG 2006)

FILE 'REGISTRY' ENTERED AT 14:59:37 ON 22 AUG 2006
EXP TIOTROPIUM/CN
L1 10 S E3-E12
EXP OXATROPIUM/CN
EXP OXITROPIUM/CN
L2 2 S E3-E4
EXP IPRATROPIUM/CN
L3 2 S E3-E4
L4 0 S CLIOMILAST/CN
EXP ARIFLO/CN
L5 1 S ARIFLO/CN
L6 1 S ENPROFYLLINE/CN
L7 1 S ROFLUMILAST/CN
L8 STRUCTURE UPLOADED
L9 0 S L8
L10 23 S L8 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:04:11 ON 22 AUG 2006
L11 881 S L1 OR L2 OR L3
L12 556 S L5 OR L6 OR L7 OR L10
L13 26 S L11 AND L12
L14 10 S L13 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONAR
L15 0 S L14 NOT PY>2001
L16 0 S L14 NOT PY>2002
L17 237 S L11 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONAR
L18 51 S L17 NOT PY>2001
L19 11 S L18 AND TIOTROPIUM
L20 0 S L19 AND ASTHSMA
L21 3 S L19 AND ASTHMA
L22 0 S L12 AND ASTHSMA AND (COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONA
L23 85 S L12 AND (COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE

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L24           14 S L23 NOT PY>2001

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
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STN INTERNATIONAL LOGOFF AT 15:12:17 ON 22 AUG 2006
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STN INTERNATIONAL LOGOFF AT 16:23:35 ON 22 AUG 2006


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 NEWS  4   APR 04  STN AnaVist $500 visualization usage credit offered
 NEWS  5   MAY 10  CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS  6   MAY 11  KOREAPAT updates resume
 NEWS  7   MAY 19  Derwent World Patents Index to be reloaded and enhanced
 NEWS  8   MAY 30  IPC 8 Rolled-up Core codes added to CA/CAplus and
                   USPATFULL/USPAT2
 NEWS  9   MAY 30  The F-Term thesaurus is now available in CA/CAplus
 NEWS 10   JUN 02  The first reclassification of IPC codes now complete in
                   INPADOC
 NEWS 11   JUN 26  TULSA/TULSA2 reloaded and enhanced with new search and
                   and display fields
 NEWS 12   JUN 28  Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 13   JUl 11  CHEMSAFE reloaded and enhanced
 NEWS 14   JUl 14  FSTA enhanced with Japanese patents
 NEWS 15   JUl 19  Coverage of Research Disclosure reinstated in DWPI
 NEWS 16   AUG 09  INSPEC enhanced with 1898-1968 archive

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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FILE 'HOME' ENTERED AT 16:24:23 ON 22 AUG 2006

=> index bioscience patents
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
FILE 'ENCOMPPAT2' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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                                                        ENTRY     SESSION
FULL ESTIMATED COST                                      0.21        0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
      AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
      CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
      DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 16:24:33 ON 22 AUG 2006

92 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (anticholinergic or antimuscarinic) and (PDE4)
          1   FILE BIOSIS
          6   FILE CAPLUS
          1   FILE DRUGU
  33 FILES SEARCHED...
         52   FILE IFIPAT
          2   FILE PHIN
          2   FILE PROMT
          6   FILE PROUSDDR
          1   FILE RDISCLOSURE
          1   FILE SCISEARCH
          1   FILE TOXCENTER
        201   FILE USPATFULL
         27   FILE USPAT2
         32   FILE WPIDS
          6   FILE WPIFV
         32   FILE WPINDEX
  69 FILES SEARCHED...
          1   FILE DPCI
         36   FILE EPFULL
         16   FILE INPADOC
        305   FILE PCTFULL

  19 FILES HAVE ONE OR MORE ANSWERS,    92 FILES SEARCHED IN STNINDEX

L1   QUE (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)

=> file uspatfull epfull pctfull
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY     SESSION
FULL ESTIMATED COST                                1.83        2.04

FILE 'USPATFULL' ENTERED AT 16:26:03 ON 22 AUG 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EPFULL' ENTERED AT 16:26:03 ON 22 AUG 2006
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FILE 'PCTFULL' ENTERED AT 16:26:03 ON 22 AUG 2006
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=> s (anticholinergic or antimuscarinic) and (PDE4)
L2          542 (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)

=> s (anticholinergic or antimuscarinic) and (PDE4(w)inhibit?)
L3          514 (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4(W) INHIBIT?)

=> s l3 not py>2001
L4            6 L3 NOT PY>2001

=> d l4 1-6 ti
```

L4 ANSWER 1 OF 6 USPATFULL on STN
TI Anti-allergy anti-inflammatory composition

L4 ANSWER 2 OF 6 EPFULL COPYRIGHT 2006 EPO/FIZ KA on STN
TIEN Prokinetic agents for treating gastric hypomotility and related disorders.
TIFR Agents prokinetiques pour le traitement de l'hypomobilite gastrique et des troubles similaires.
TIDE Prokinetische Arzneimittel zur Behandlung von Magen Hypomobilitaets- und vergleichbaren Erkrankungen.

L4 ANSWER 3 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN THE TREATMENT OF RESPIRATORY DISEASES
TIFR TRAITEMENT DE TROUBLES RESPIRATOIRES

L4 ANSWER 4 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN NICOTINAMIDE BENZOFUSED-HETEROCYCLYL DERIVATIVES USEFUL AS SELECTIVE INHIBITORS OF PDE4 ISOZYMES
TIFR DERIVES BENZOCONDENSES HETEROCYCLIQUES DE NICOTINAMIDE UTILES COMME INHIBITEURS SELECTIFS D'ISOZYMES PDE4

L4 ANSWER 5 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN PYRIMIDINE CARBOXAMIDES USEFUL AS INHIBITORS OF PDE4 ISOZYMES
TIFR CARBOXAMIDES DE PYRIMIDINE UTILISES COMME INHIBITEURS DES ISOZYMES PDE4

L4 ANSWER 6 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN INDAZOLE BIOISOSTERE REPLACEMENT OF CATECHOL IN THERAPEUTICALLY ACTIVE COMPOUNDS
TIFR REMPLACEMENT BIOISOSTHERE DU CATECHOL PAR L'INDAZOLE DANS DES COMPOSES THERAPEUTIQUEMENT ACTIFS

=> d l4 1-6 ti abs bib

L4 ANSWER 1 OF 6 USPATFULL on STN
TI Anti-allergy anti-inflammatory composition
AB A novel composition of Nimesulide and salts thereof and Cetrizine possessing antileukotriene, antihistaminic, antiallergic and antiinflammatory action is disclosed. The composition is useful in the cure of allergic disorders such as rhinitis, bronchitis, asthama, urticaria and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2001:107898 USPATFULL
TI Anti-allergy anti-inflammatory composition
IN Singh, Amarjit, New Delhi, India
Jain, Rajesh, New Delhi, India
PA Panacea Biotec Limited, New Delhi, India (non-U.S. corporation)
PI US 6258816 B1 20010710
AI US 1998-178652 19981026 (9)
PRAI IN 1997-318597 19971106
DT Utility
FS GRANTED
EXNAM Primary Examiner: Geist, Gary; Assistant Examiner: White, Everett
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 681
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 2 OF 6 EPFULL COPYRIGHT 2006 EPO/FIZ KA on STN
TIEN Prokinetic agents for treating gastric hypomotility and related disorders.
TIFR Agents prokinetiques pour le traitement de l'hypomobilite gastrique et

des troubles similaires.
TIDE Prokinetische Arzneimittel zur Behandlung von Magen Hypomobilitaets- und vergleichbaren Erkrankungen.

ABEN

The invention describes the use of PDE-4 (phosphodiesterase-4) inhibitors in the treatment or prevention of gastric stasis resulting from hypomotility of the stomach (with delayed emptying of the liquid and/or solid contents of the stomach).

More particularly said inhibitors are indazole derivatives such as (1H-indazol-6-yl)-cyclohexane or cyclohexene carboxylic acid derivatives, carbonitriles, amides or esters thereof. Gastric or gastrointestinal disorders, which may also be caused by adverse effects of therapeutic agents, of surgical operations or concomitant or secondary aspects of another disease, which include pain, nausea, vomiting, heartburn, postprandial discomfort, indigestion and gastro-esophageal reflux, can be prevented or treated with pharmaceutical compositions containing said PDE-4 indazole inhibitors.

AN 1999:109036 EPFULL
DUPD 20001018 DUPW 200042
TIEN Prokinetic agents for treating gastric hypomotility and related disorders.
TIFR Agents prokinetiques pour le traitement de l'hypomobilite gastrique et des troubles similaires.
TIDE Prokinetische Arzneimittel zur Behandlung von Magen Hypomobilitaets- und vergleichbaren Erkrankungen.
IN Watson, John Wesley, 13 Cranwood Road, Ledyard, Connecticut 06339, US;
Woods, Anthony John, Wellcome Trust, 183 Euston Road, London NW1 2BN, GB;
Andrews, Paul, St. Georges Hospital Med. School, Department Physiology, Cranmer Terrace, Tooting, London SW17 0RE, GB
PA PFIZER INC., 235 East 42nd Street, New York, N.Y. 10017, US
PAN 200961
AG Simpson, Alison Elizabeth Fraser, et al, Urquhart-Dykes & Lord, 30 Welbeck Street, London W1M 7PG, GB
AGN 77401
DT Patent
LAF English
LA English
LAP English
TL German; English; French
PIT EPA3 Separate publication of search report
PI EP 1040829 A3 20001018
DS AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
EXTENSION STATES: AL LT LV MK RO SI
AI EP 1999-310202 A 19991216
PRAI US 1998-114217P P 19981230

L4 ANSWER 3 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN THE TREATMENT OF RESPIRATORY DISEASES
TIFR TRAITEMENT DE TROUBLES RESPIRATOIRES
ABEN A pharmaceutical composition for pulmonary delivery comprises glycopyrrolate in a controlled release formulation, wherein, on administration, the glycopyrrolate exerts its pharmacological effect over a period greater than 12 hours.
ABFR La presente invention concerne une composition pharmaceutique destinee a une administration pulmonaire, comprenant du glycopyrrolate dans une formulation a liberation controlee. Lorsque ladite composition a ete administree, le glycopyrrolate exerce son action pharmacologique pendant une periode superieure a 12 heures.
AN 2001076575 PCTFULL ED 20020822
TIEN THE TREATMENT OF RESPIRATORY DISEASES
TIFR TRAITEMENT DE TROUBLES RESPIRATOIRES

IN BANNISTER, Robin, Mark;
RICHARDS, Andrew, John, McGlashan;
GILBERT, Julian, Clive;
MORTON, David, A., V.;
STANIFORTH, John
PA ARAKIS LTD.;
BANNISTER, Robin, Mark;
RICHARDS, Andrew, John, McGlashan;
GILBERT, Julian, Clive;
MORTON, David, A., V.;
STANIFORTH, John
DT Patent
PI WO 2001076575 A2 20011018
DS W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU
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ML MR NE SN TD TG
AI WO 2001-GB1606 A 20010409
PRAI GB 2000-0008660.3 20000407

L4 ANSWER 4 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN NICOTINAMIDE BENZOFUSED-HETEROCYCLYL DERIVATIVES USEFUL AS SELECTIVE INHIBITORS OF PDE4 ISOZYMES
TIFR DERIVES BENZOCONDENSES HETEROCYCLIQUES DE NICOTINAMIDE UTILES COMME INHIBITEURS SELECTIFS D'ISOZYMES PDE4
ABEN Compounds useful as inhibitors of PDE4 in the treatment of diseas s regulated by the activation and degranulation of eosinophils, especially asthma, chronic bronchitis, and chronic obstructive pulmonary disease, of Formula (1.0.0.). In said formula R5 and R6 are taken together to form a moiety of partial Formulas (1.1.1) through (1.1.5) or a pharmaceutically acceptable salt thereof.
ABFR L'invention a trait a des composes utiles comme inhibiteurs de PDE4 dans le traitement de maladies regulees par l'activation et la degranulation de polynucleaires eosinophiles, specialement l'asthme, la bronchite chronique et la bronchopneumopathie obstructive chronique ; ou a un sel pharmaceutiquement acceptable de ces composes. Les composes sont representes par la formule (1.0.0), dans laquelle R5 et R6 forment ensemble une fraction des formules partielles (1.1.1) a (1.1.5).
AN 2001057036 PCTFULL ED 20020827
TIEN NICOTINAMIDE BENZOFUSED-HETEROCYCLYL DERIVATIVES USEFUL AS SELECTIVE INHIBITORS OF PDE4 ISOZYMES
TIFR DERIVES BENZOCONDENSES HETEROCYCLIQUES DE NICOTINAMIDE UTILES COMME INHIBITEURS SELECTIFS D'ISOZYMES PDE4
IN MARFAT, Anthony;
CHAMBER, Robert, James
PA PFIZER PRODUCTS INC.;
MARFAT, Anthony;
CHAMBER, Robert, James
DT Patent
PI WO 2001057036 A1 20010809
DS W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ
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GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML
MR NE SN TD TG
AI WO 2001-IB124 A 20010130
PRAI US 2000-60/179,284 20000131

L4 ANSWER 5 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN PYRIMIDINE CARBOXAMIDES USEFUL AS INHIBITORS OF PDE4 ISOZYMES
TIFR CARBOXAMIDES DE PYRIMIDINE UTILISES COMME INHIBITEURS DES ISOZYMES PDE4
ABEN Compounds of formula (1.0.0) are described, as well as the usefulness of a pharmaceutical composition for treating inflammatory, respiratory and allergic diseases and conditions, especially asthma; chronic obstructive pulmonary disease (COPD) including chronic bronchitis, emphysema, and bronchiectasis; chronic rhinitis; and chronic sinusitis.
ABFR L'invention concerne des composes correspondant a la formule (1.0.0) ainsi que l'utilisation d'une composition pharmaceutique dans le traitement des maladies et etats inflammatoires, respiratoires et allergiques et notamment de l'asthme; de la BPCO (broncho-pneumopathie chronique obstructive), y compris la bronchite chronique, l'emphyseme et la bronchectasie, la rhinite chronique et la sinusite chronique.
AN 2001057025 PCTFULL ED 20020827
TIEN PYRIMIDINE CARBOXAMIDES USEFUL AS INHIBITORS OF PDE4 ISOZYMES
TIFR CARBOXAMIDES DE PYRIMIDINE UTILISES COMME INHIBITEURS DES ISOZYMES PDE4
IN CHAMBERS, Robert, James;
MAGEE, Thomas, Victor;
MARFAT, Anthony
PA PFIZER PRODUCTS INC.;
CHAMBERS, Robert, James;
MAGEE, Thomas, Victor;
MARFAT, Anthony
DT Patent
PI WO 2001057025 A1 20010809
DS W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
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MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA
UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW
AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB
GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML
MR NE SN TD TG
AI WO 2001-IB125 A 20010130
PRAI US 2000-60/179,282 20000131

L4 ANSWER 6 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN INDAZOLE BIOISOSTERE REPLACEMENT OF CATECHOL IN THERAPEUTICALLY ACTIVE COMPOUNDS
TIFR REMPLACEMENT BIOISOSTHERE DU CATECHOL PAR L'INDAZOLE DANS DES COMPOSES THERAPEUTIQUEMENT ACTIFS
ABEN Therapeutically active compositions of matter and member species thereof are described which
comprise indazole-containing compounds, said compounds and their therapeutic activity resulting
directly from an indazole-for-catechol bioisostere replacement of a catechol-containing compound
having the same therapeutic activity, where non-catechol substituents are the same or homologous
before and after said replacement, and wherein said compositions of matter comprise a compound of
Formula (I1¿) or (I2¿), or a pharmaceutically acceptable salt thereof, wherein in a preferred
embodiment RC¿ is hydrogen; RA¿ is cyclohexyl; and RB¿ is ethyl. R¿a and R¿b are each individually and independently hydrogen or non-catechol substituents of said compounds resulting directly from an
indazole-for-catechol bioisotere replacement of said catechol-containing compound having said
therapeutic activity, where said non-catechol substituents are the same or homologous before and
after said replacement, provided that both of R¿a and R¿b cannot be hydrogen at the same time. The
therapeutic activity involved may comprise cholinesterase inhibitory

activity, adrenergic
α¿1-antagonist and β¿1-agonist activity,
calcium channel inhibitory activity,
antineoplastic activity, and phosphodiesterase type IV inhibitor
activity.

ABFR La presente invention concerne, d'une part des compositions
therapeutiquement actives a base de
substances et d'especes appartenant a ces substances, lesquelles
compositions comprennent des
composes contenant de l'indazole, ou d'autre part certains des sels
derives pharmaceutiquement
admis. En l'occurrence, les composes consideres, et leur activite
therapeutique, resultent
directement d'un remplacement bioisosthere du catechol par l'indazole
dans des composes contenant du
catechol et presentant la meme activite therapeutique, les substituants
non-catechol etant les memes
ou homologues avant et apres ledit remplacement. Les compositions a base
de la substance consideree
comprennent un compose represente par la formule generale (I?1¿)
ou (I?2¿). Dans une realisation
preferee, R?C¿ est hydrogene, R?A¿ est cyclohexyle, et
R?B¿ est ethyle. R¿a? et R¿b? sont chacun
individuellement et independamment hydrogene ou substituant non catechol
des composes consideres
resultant directement d'un remplacement bioisosthere du catechol par
l'indazole dans le compose
considere contenant du catechol et presentant une activite
therapeutique. En l'occurrence, lesdits
substituants non catechol sont les memes ou homologue avant et apres le
remplacement considere, sous
la reserve que R¿a? et R¿b? ne soient pas en meme temps
hydrogene. L'activite therapeutique
consideree peut etre une activite inhibitrice de la cholinesterase, une
activite adrenergique
α¿1?-antagoniste et β¿1?-agoniste, une activite
inhibitrice du canal calcium, une
activite antineoplasique, voire une activite inhibitrice des
phosphodiesterases de type IV.

AN 1999023077 PCTFULL ED 20020515

TIEN INDAZOLE BIOISOSTERE REPLACEMENT OF CATECHOL IN THERAPEUTICALLY ACTIVE
COMPOUNDS

TIFR REMPLACEMENT BIOISOSTHERE DU CATECHOL PAR L'INDAZOLE DANS DES COMPOSES
THERAPEUTIQUEMENT ACTIFS

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PA PFIZER PRODUCTS INC.;
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LA English
DT Patent
PI WO 9923077 A1 19990514
DS W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES
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SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS
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DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM
GA GN GW ML MR NE SN TD TG
AI WO 1998-IB1710 A 19981026
PRAI US 1997-60/064,229 19971104
US 1997-60/064,187 19971104
US 1997-60/064,024 19971104
US 1997-60/064,228 19971104
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     AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
     CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
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              6   FILE CAPLUS
              1   FILE DRUGU
             52   FILE IFIPAT
              2   FILE PHIN
              2   FILE PROMT
              6   FILE PROUSDDR
              1   FILE RDISCLOSURE
              1   FILE SCISEARCH
              1   FILE TOXCENTER
            201   FILE USPATFULL
             27   FILE USPAT2
             32   FILE WPIDS
              6   FILE WPIFV
             32   FILE WPINDEX
              1   FILE DPCI
             36   FILE EPFULL
             16   FILE INPADOC
            305   FILE PCTFULL
L1             QUE (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)
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     FILE 'USPATFULL, EPFULL, PCTFULL' ENTERED AT 16:26:03 ON 22 AUG 2006
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L3          514 S (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4(W)INHIBIT?)
L4            6 S L3 NOT PY>2001

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